REMARKS

Entry of the foregoing and further and favorable reconsideration of the subject application are respectfully requested, in light of the following remarks pursuant to and consistent with 37 C.F.R. §1.112.

By the present amendment, the specification has been amended to correct the translation of the R^1 group to match that of original German PCT text. Support for the amendment can be found in the originally filed German application received by the Patent and Trademark Office on September 14, 2001 (see Notice of Acceptance of Aplication Under 35 U.S.C. § 371 and 37 C.F.R. §§ 1.494 or 1.495 mailed on October 5, 2001). Claims 9 and 10 have been canceled without prejudice or disclaimer to the subject matter recited therein, and claims 1, 7, 11 and 12 have been amended to further clarify Applicants' invention. Support for amended claim 1 can be found in the originally filed German application received by the Patent and Trademark Office on September 14, 2001 (see Notice of Acceptance of Aplication Under 35 U.S.C. § 371 and 37 C.F.R. §§ 1.494 or 1.495 mailed on October 5, 2001). Claim 1 has been reworded for clarity in the definition of R^1. No new matter has been added.

I. Rejections Under 35 U.S.C. §§ 112, second paragraph, and 101

Claims 1, 2, 7 and 9-12 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

Claims 9 and 10 have been rejected for being substantial duplicates of claim cliam 8. This rejection is rendered moot in light of the cancellation of claims 9 and 10.

Claims 7, 11 and 12 have been rejected under 35 U.S.C. § 112, second paragraph, and 35 U.S.C. § 101 for reciting "use" of the compounds of the invention without setting forth any steps involved in the process. This rejection is rendered moot in light of the amendments to claims 7, 11 and 12. Specifically, claims 7, 11 and 12 have been amended to recite the appropriate steps in the methods.

The other aspects of the rejection have been overcome by restoring the correct German language scope of R^1.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 7 and 9-12 under 35 U.S.C. § 112.

II. Rejections Under 35 U.S.C. § 102

Claims 1-6 and 8 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ozaki et al. (U.S. Patent No. 5,716,993). Applicants respectfully traverse this rejection.

This rejection has been rendered moot in view of the amendment to claim 1. No new matter is involved. See MPEP §2173.05(i).

Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-6 and 8 under 35 U.S.C. § 102(b).

Claims 1-6 and 8 have also been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Schipper et al. (U.S. Patent No. 3,226,394). Applicants respectfully traverse this rejection.

This rejection is rendered moot in view of the reinstatement of the correct German language claim scope.

Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-6 and 8 under 35 U.S.C. § 102(b).

III. Rejections Under 35 U.S.C. § 103

Claims 1-6 and 8 have also been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ozaki et al. (U.S. Patent No. 5,716,993). Applicants respectfully traverse this rejection.

The present invention provides derivatives of anthranilic acid amides which inhibit VEGF tyrosine kinase and the present invention provides pharmaceutical agents for the treatment of diseases triggered by persistent angiogenesis, *e.g.*, psoriasis, arthritis, hemangioma, angiofibroma, eye diseases, renal diseases and other VEGF-induced pathological angiogenesis and vascular permeable conditions, such as tumor vascularization, etc. (see page 1, third paragraph of the specification).

Ozaki et al., however, discloses compounds which inhibit cGMP phosphodiesterase and therefore have a relaxing effect on the vascular system (see column 1, lines 27-29 and 43-51 of Ozaki et al.). Ozaki et al. suggests using the derivatives to treat angina pectoris or various ischemic heart diseases (see column 1, lines 47-50, of Ozaki et al.).

Schipper et al. discloses derivatives having an activity on the central nervous system (see column 1, lines 38-40, of Schipper et al.). Column 1, lines 42-44, of Schipper et al. refers to the potentiation of the hypnotic effect and to the suppression of convulsant action. Further, Schipper et al. discloses that the derivatives may be useful as an anti-Parkinsons drug.

Therefore, Applicants submit that a person skilled in the art would not be motivated from these references to use the claimed compounds or any others for the purpose of method claims 11 and 12.

For the compounds themselves, as can be seen from the forgoing, Schipper discloses compounds having structural features which exclude those of this invention. There is nothing in Schipper which would motivate a skilled worker to make the changes necessary to the references

compounds in order to arrive the claimed compounds. Without such motivation, there can be no obviousness. *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

As for the disclosure of Ozaki et al, mere possible overlap does not establish obviousness. The Meock v. Biocraft decision cited by the Examiner has been explicitly stated not to hold that overlap always establishes obviousness. See *In re Baird*, 16 F.2d 380, 29 USPQ2d 1550 (Fed. Cir. 1994). In Baird, a very broad disclosure, similar to that in Ozaki et al., was held not to render obvious all the compounds included within the scope of its very broad Markush disclosure. Rather, the only portion of the reference which could realistically teach a skilled worker anything of significance, was found to be its examples. All of these taught away from the claims of the Baird et al. application. Consequently, the broad prior art disclosure did not render the claims obvious.

The same thing is true here, where all of the examples of those of Ozaki et al. are directed away from the claimed invention. Consequently, Ozaki et al. does not render the claims obvious.

As can be seen, even the combination of the two references would not render the claims obvious for reasons analogous to those stated above with respect to the references singly.

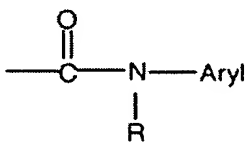
Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-6 and 8 under 35 U.S.C. § 103(a).

IV. Double Patenting Rejection

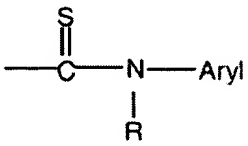
Claims 1-12 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application Serial No. 09/850,434 (WO 00/27820). Applicants respectfully traverse this rejection.

The above translation fix eliminates the apparent overlap at issue.

In WO 00/27820, R is equivalent to Z-R' of the present application. There, W can be =O or =S, and R_1 aryl must be directly connected to -NR, (shown in formulas Ia, Ib below).

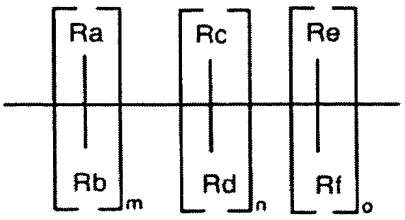


Ia)



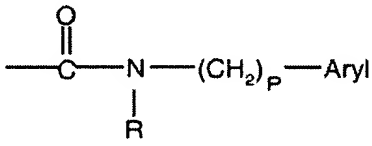
Ib)

However, in the present application, when W is =O or =S and A is NR^2 then R^1 cannot be aryl (or heteroaryl) directly bonded to NR^2. Rather, R^1 is bonded to A via Z, which can be =NR10, =N(R10)-(CH2)q-, branched or unbranched C_{1-6} alkyl or the group

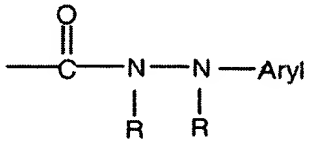


II)

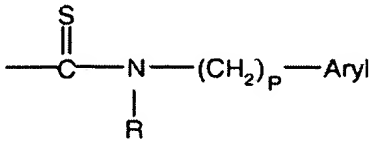
or in the case where A, Z and R^1 form a shared group, then the aryl is as well NOT directly connected to the =N- (as shown in formulas III a-d).



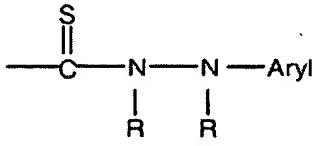
IIIa)



IIIb)



IIIc)



IIId)

Therefore, Applicants submit that there is no double patenting. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1-12 under the judicially created doctrine of obviousness-type double patenting.

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

for

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Filed: November 12, 2002

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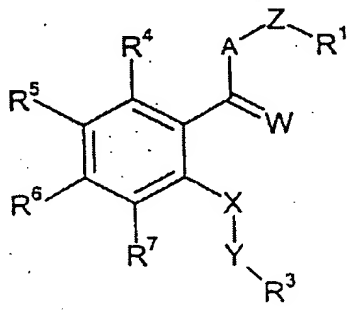
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

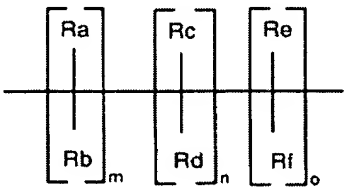
--It has now been found that compounds of general formula I



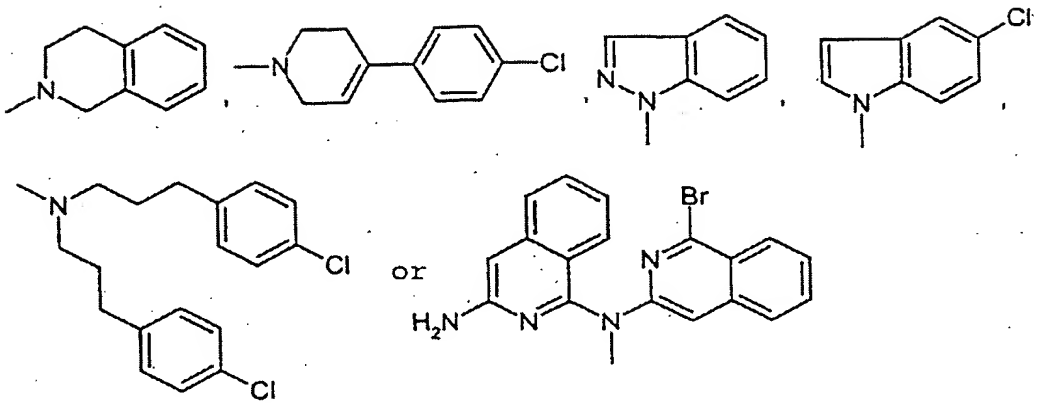
I

in which

A	stands for the group $=NR^2$,
W	stands for oxygen, sulfur, two hydrogen atoms or the group $=NR^8$,
Z	stands for the group $=NR^{10}$ or =N-,
	$-N(R^{10})-(CH_2)_q-$, branched or unbranched C_{1-6} alkyl or the group



or A, Z and R^1 together form the group



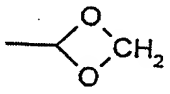
m, n and o	stand for 0-3,
q	stands for 1-6,
R_a, R_b, R_c, R_d, R_e, R_f,	independently of one another, stand for hydrogen, C_{1-4} alkyl or the group $=NR^{10}$, and/or R_a and/or R_b can form a bond with R_c and/or R_d or R_c can form a bond with R_e and/or R_f or up to two of radicals R_a-R_f can close a bridge with up to 3 C-atoms each to form R^1 or R^2,
X	stands for the group $=NR^9$ or =N-,
Y	stands for the group $-(CH_2)_p$,
p	stands for 1-4,
R^1	~~stands for C_{1-6} alkyl that is unsubstituted or is optionally substituted in one or more places with halogen, C_{1-6} alkyl, in one or more places with halogen, or aryl or heteroaryl that is substituted with C_{1-6} alkoxy, with the exception of compounds in which aryl is bonded right in the $=NR^2$ group in the meaning of A~~ stands for unsubstituted or, optionally, one or more times with halogen, C_{1-6} alkyl, one or more times with halogen substituted C_{1-6} alkyl or C_{1-6} alkoxy substituted

aryl or heteroaryl, with the exception of compounds in which aryl is bonded directly to the $=NR^2$ group in the meaning of A,

R^2 stands for hydrogen or C_{1-6} alkyl or forms a bridge with up to 3 ring members with R_a-R_f from Z or to form R_1,

R^3 stands for monocyclic or bicyclic aryl or heteroaryl that is unsubstituted or optionally substituted in one or more places with halogen, C_{1-6} alkyl, C_{1-6} alkoxy or hydroxy,

R^4, R^5, R^6, and R^7, independently of one another, stand for hydrogen, halogen, or C_{1-6} alkoxy, C_{1-6} alkyl or C_{1-6} carboxylalkyl that is unsubstituted or optionally substituted in one or more places with halogen, or R^5 and R^6 together form the group

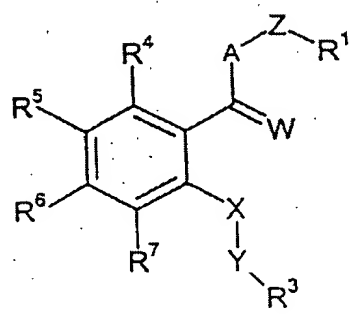


R^8, R^9, and R^{10}, independently of one another, stand for hydrogen or C_{1-6} alkyl,

as well as their isomers and salts, stop a tyrosine phosphorylation or persistent angiogenesis and thus prevent the growth and propagation of tumors.--

IN THE CLAIMS

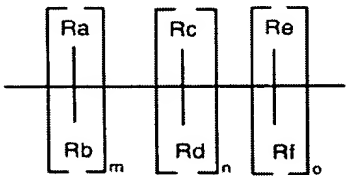
1. (Amended) A ~~Compounds~~ compound of ~~general~~ formula I



I

in which

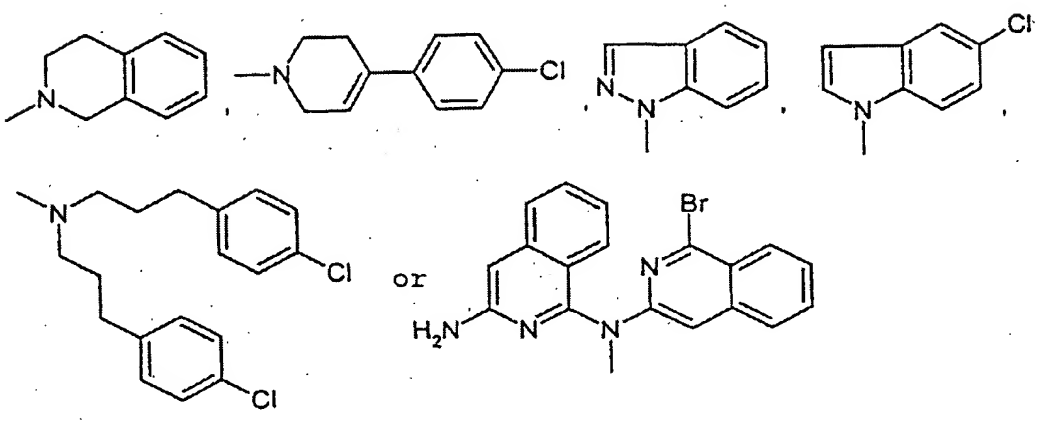
A	stands for the group $=NR^2$,
W	stands for oxygen, sulfur, two hydrogen atoms or the group $=NR^8$,
Z	stands for the group $=NR^{10}$ or =N-,
	$-N(R^{10})-(CH_2)_q-$, branched or unbranched C_{1-6} alkyl or the group



or A, Z

and R^1

together form the group



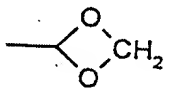
m, n and o	stand for 0-3,
q	stands for 1-6,
R_a, R_b, R_c, R_d, R_e, R_f,	independently of one another, stand for hydrogen, C_{1-4} alkyl or the group $=NR^{10}$, and/or R_a and/or R_b can form a bond with R_c and/or R_d or R_c can form a bond with R_e and/or R_f or up to two of radicals R_a-R_f can close a bridge with up to 3 C-atoms each to form R^1 or R^2,
X	stands for the group $=NR^9$ or =N-,
Y	stands for the group $-(CH_2)_p$,
p	stands for 1-4,
R^1	~~stands for C_{1-6} alkyl that is unsubstituted or is optionally substituted in one or more places with halogen, C_{1-6} alkyl, in one or more places with halogen, or aryl or heteroaryl that is substituted with C_{1-6} alkoxy, with the exception of compounds in which aryl is bonded right in the $=NR^2$ group in the meaning of A~~ stands for unsubstituted aryl or heteroaryl, or for aryl or heteroaryl substituted one or more times with halogen; C_{1-6} alkyl; or one or more times with halogen substituted C_{1-6}

alkyl or C_{1-6} alkoxy; with the proviso that R^1 is not aryl directly bonded to $=NR^2$ in the meaning of A,

R^2 stands for hydrogen or C_{1-6} alkyl or forms a bridge with up to 3 ring members with R_a-R_f from Z or to form R_1,

R^3 stands for monocyclic or bicyclic aryl or heteroaryl that is unsubstituted or optionally substituted in one or more places with halogen, C_{1-6} alkyl, C_{1-6} alkoxy or hydroxy,

R^4, R^5, R^6, and R^7, independently of one another, stand for hydrogen, halogen, or C_{1-6} alkoxy, C_{1-6} alkyl or C_{1-6} carboxylalkyl that is unsubstituted or optionally substituted in one or more places with halogen, or R^5 and R^6 together form the group



R^8, R^9, and R^{10}, independently of one another, stand for hydrogen or C_{1-6} alkyl,

~~as well as their~~ or an isomer ~~isomers~~ or, pharmaceutically acceptable salt thereof ~~and salts~~ with the proviso that when A is $=NR^2$, X is $=NR^9$, $R^{2,4,6,7,9}$ is H, R^5 is Cl, W is O, Z=Y is $-CH_2-$, and R^3 is 4-pyridyl, then R^1 is not 3,4-methylendioxybenzyl.

7. (Amended) ~~Use of the compounds of general formula I, according to claim 1, for the production of a pharmaceutical agent~~ A method of claim 11 for the treatment of tumors, psoriasis, arthritis ~~, such as rheumatoid arthritis~~, hemangioma, angiofibroma, eye diseases ~~, such as diabetic retinopathy~~, neovascular glaucoma, renal diseases ~~, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombic microangiopathic syndrome, transplant rejections and glomerulopathy~~, fibrotic diseases ~~, such as cirrhosis of the liver~~, mesangial-cell-proliferative diseases, arteriosclerosis, injuries to the nerve tissue, and for inhibiting the reocclusion of vessels after balloon

catheter treatment, in vascular prosthetics or after mechanical devices are used to keep vessels open ; ~~such as, e.g., stents comprising administering to a patient in need thereof a therapeutically affective amount of a pharmaceutical agent comprising a compound of claim 1~~.

8. (Amended) A ~~Pharmaceutical~~ pharmaceutical ~~agent that contains~~ composition comprising a therapeutical effective amount of at least one compound according to claim 1 and a pharmaceutical acceptable carrier.

9. (Amended) A ~~Pharmaceutical~~ pharmaceutical composition ~~agent~~ according to claim 8 for the treatment of tumors, psoriasis, arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, renal diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosisk, thrombic microangiopathic syndrome, transplant rejections and glomerulopathy, fibrotic diseases, such as cirrhosis of the liver, mesangial-cell-proliferative diseases, arteriosclerosis, injuries to the nerve tissue, and for inhibiting the reocclusion of vessels after baloon catheter treatment, in vascular prosthetics or after mechanical devices are used to keep vessels open, such as, e.g., stents..

11. (Amended) ~~Use of the compounds of formula I according to claim 1 as inhibitors of~~ A method of inhibiting the tyrosine ~~kinases~~ kinase KDR and/or FLT, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.

12. (Amended) ~~Use of the compounds of general formula I according to claim 1 in the form of a pharmaceutical preparation~~ A method of producing a pharmaceutical preparation for enteral, parenteral and oral administration comprising mixing a compound of claim 1 with a suitable pharmaceutical carrier.